Author Search

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=> FILE CASREACT
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FILE CONTENT:1840 - 11 Aug 2007 VOL 147 ISS 8

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*************************************************************
*                                                           *
*     CASREACT now has more than 12 million reactions       *
*                                                           *
*************************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.


=> D QUE L25
L15             STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation:
Uploading strG.str
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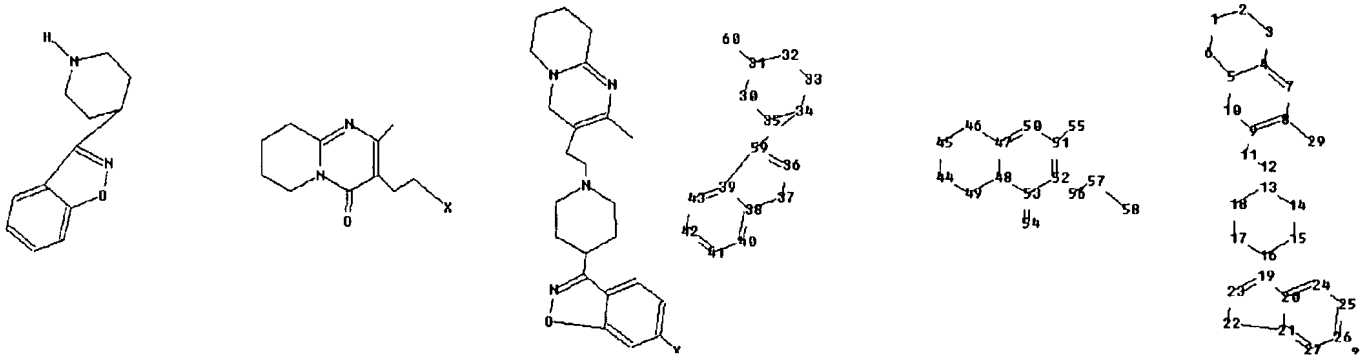

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ring nodes :
1  2  3  4  5  6  7  8  9  10  13  14  15  16  17  18  19  20  21  22  23  24  25
26  27  30  31  32  33  34  35  36  37  38  39  40  41  42  43  44  45  46  47  48
49  50  51  52
53  59
chain bonds :
8-29  9-11  11-12  12-13  16-19  26-28  31-60  34-59  51-55  52-56  53-54  56-57
57-58
```

```
ring bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10  13-14  13-18  14-15  15-16
16-17  17-18  19-20  19-23  20-21  20-24  21-22  21-27  22-23  24-25  25-26  26-27
30-31  30-35
31-32  32-33  33-34  34-35  36-37  36-59  37-38  38-39  38-40  39-43  39-59  40-41
41-42  42-43
44-45  44-49  45-46  46-47  47-48  47-50  48-49  48-53  50-51  51-52  52-53
exact/norm bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10  12-13  13-14  13-18  14-15
15-16  16-17  17-18  19-20  19-23  21-22  22-23  30-31  30-35  31-32  32-33  33-34
34-35  36-37
36-59  37-38  39-59  44-45  44-49  45-46  46-47  47-48  47-50  48-49  48-53  50-51
51-52  52-53
53-54
exact bonds :
8-29  9-11  11-12  16-19  26-28  31-60  34-59  51-55  52-56  56-57  57-58
normalized bonds :
20-21  20-24  21-27  24-25  25-26  26-27  38-39  38-40  39-43  40-41  41-42  42-43


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
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fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 30
containing 44


L21            8 SEA FILE=CASREACT SSS FUL L15 (     9 REACTIONS)
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L23          108 SEA FILE=CASREACT ABB=ON  PLU=ON  KUMAR B?/AU
L24           20 SEA FILE=CASREACT ABB=ON  PLU=ON  MANJUNATHA S?/AU
L25            1 SEA FILE=CASREACT ABB=ON  PLU=ON  (L22 OR L23 OR L24) AND L21


=> D IBIB AB CRD L25 1


L25  ANSWER 1 OF 1  CASREACT  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         142:355280  CASREACT  Full-text
TITLE:                    A process for preparation of risperidone, useful as
                          serotonin/dopamine antagonist
INVENTOR(S):              Srinivasa, Rao Guntu; Prasanna Kumar, Basavapatna N.;
                          Manjunatha, Sulur G.; Kulkarni, Ashok Krishna
PATENT ASSIGNEE(S):       Jubilant Organosys Ltd., India
SOURCE:                   PCT Int. Appl., 25 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
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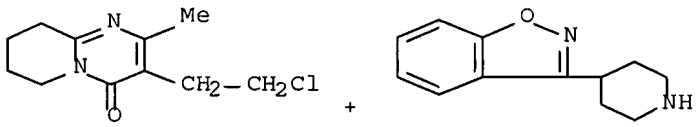
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005030772	A1	20050407	WO 2004-IN303	20040924
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003DE01209	A	20050527	IN 2003-DE1209	20030926
AU 2004276092	A1	20050407	AU 2004-276092	20040924
CA 2540360	A1	20050407	CA 2004-2540360	20040924
EP 1670797	A1	20060621	EP 2004-787585	20040924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
IN 2006DN02008	A	20070615	IN 2006-DN2008	20060412
US 2007179163	A1	20070802	US 2006-572829	20061113
PRIORITY APPLN. INFO.:			IN 2003-DE1209	20030926
			WO 2004-IN303	20040924

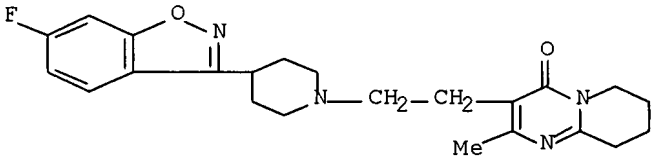
AB The invention relates to a process for preparation of risperidone (I) via condensation reaction of 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole monohydrochloride (II•HCl) with 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2,a]pyrimidin-4-one monohydrochloride (III•HCl). For instance, risperidone was prepared by the above method at 65-70 °C in water/DMF with a yield of 75% (purity: 99.87%).

RX(1) OF 6



HCl HCl

Na2CO3, Water, MeCN



81%

NOTE: optimization study
CON: STAGE(1) 30 deg C -> 70 deg C; 4 hours, 65 - 70 deg C; 4 hours, 65 - 70 deg C

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> D QUE L21
L15             STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.
L21           8 SEA FILE=CASREACT SSS FUL L15 (     9 REACTIONS)



=> D IBIB AB CRD L26 1-7


L26  ANSWER 1 OF 7  CASREACT  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         144:150381  CASREACT  Full-text
TITLE:                    A process for the preparation of risperidone
INVENTOR(S):              Czibulsa, Laszlo; Turcsanyi, Peter; Feher, Krisztina;
                          Sebok, Ferenc; Szabo, Gyoergy; Werkne Papp, Eva
PATENT ASSIGNEE(S):       Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE:                   PCT Int. Appl., 15 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     WO 2006005974      A1   20060119       WO 2005-HU72     20050706
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     HU 200401379       A2   20060228       HU 2004-1379     20040708
     HU 200401379       A3   20060428
     EP 1763529         A1   20070321       EP 2005-763422   20050706
         R:  AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR
     CN 1984913         A    20070620       CN 2005-80023096 20050706
     IN 2007KN00191     A    20070629       IN 2007-KN191    20070116
PRIORITY APPLN. INFO.:                      HU 2004-1379     20040708
                                            WO 2005-HU72     20050706
AB   The invention relates to a process for the preparation of risperidone (I) by
     reacting (chloroethyl)pyrido[1,2-a]pyrimidinone II piperidinylbenzisoxazole
     III, in which the reaction is carried out in dry methanol solvent under
     pressure, at 65-90°, the product is recovered by using a methanol/water
     mixture of specified ratio and if desired is recrystd. from an alc.
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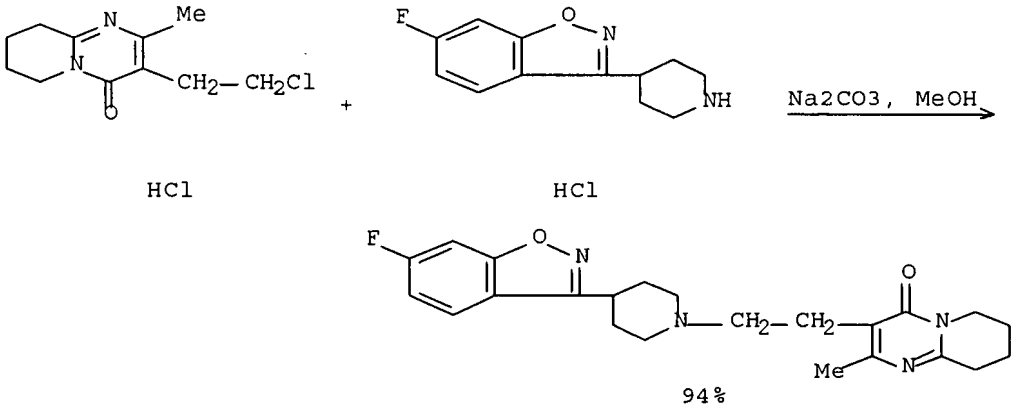
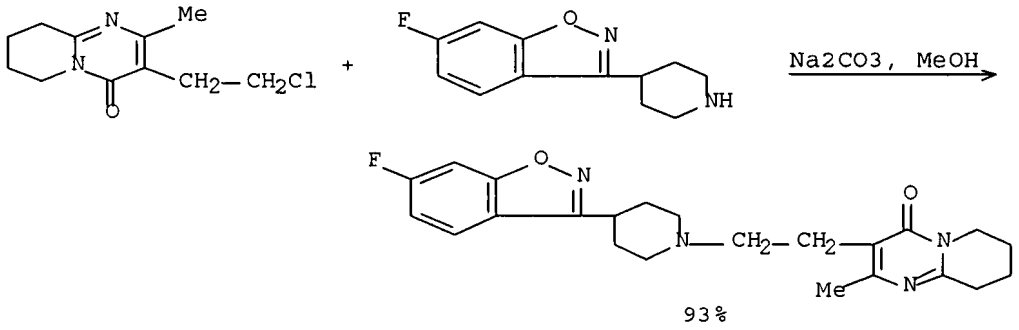
RX(1) OF 2



CON: 4 - 4.5 hours, 73 - 75 deg C

RX(2) OF 2



CON: 4 - 4.5 hours, 73 - 75 deg C

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 2 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	144:108338 CASREACT Full-text
TITLE:	Condensation process for the preparation of pure 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one
INVENTOR(S):	Reddy, Buchi Reddy; Sudhakar, Sunkari; Chakka, Ramesh; Reddy, Tamma Ranga; Kumar, Kandirelli Venkata Kiran
PATENT ASSIGNEE(S):	Dr. Reddy's Laboratories Limited, India; Dr. Reddy's Laboratories, Inc.
SOURCE:	U.S. Pat. Appl. Publ., 7 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

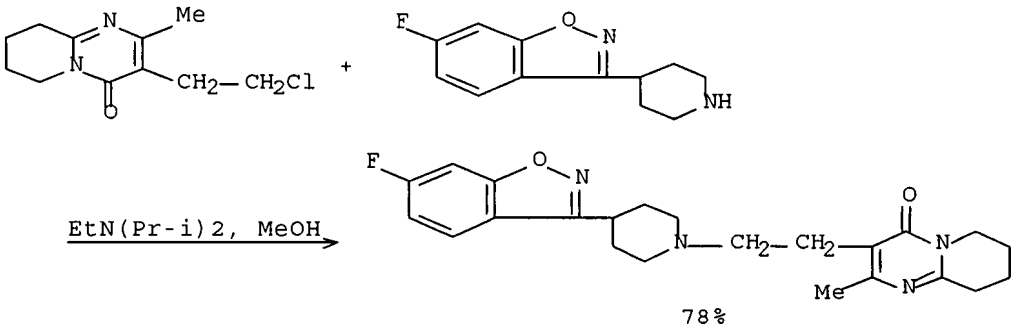
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006004199	A1	20060105	US 2004-883579	20040701

PRIORITY APPLN. INFO.: US 2004-883579 20040701

AB A process for the preparation of high-purity 3-[2-[4-(6-fluoro-1,2-benzisoxazol- 3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2- a]pyrimidin-4-one (i.e., risperidone) is presented which is based on the condensation of 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one with 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole in a lower alc. (e.g., methanol).

RX(1) OF 1



78%

CON: 70 - 100 hours, 45 - 50 deg C

L26 ANSWER 3 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 138:401742 CASREACT Full-text

TITLE: Improved process for the preparation of 3-{2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl}-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (Risperidone)

INVENTOR(S): Pongo, Laszlo; Reiter, Jozsef; Simig, Gyula; Berecz, Gabor; Clementis, Gyorgy; Slegel, Peter; Szilagyi, Janos; Koncz, Laszlo; Vereczkeyne Donath, Gyorgyi; Nagy, Kalman; Koertvelyessy, Gyulane

PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.

SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003042212	A1	20030522	WO 2002-HU120	20021113

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
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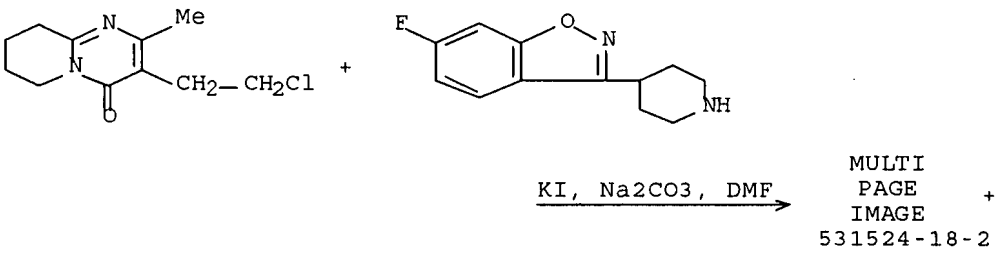
CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

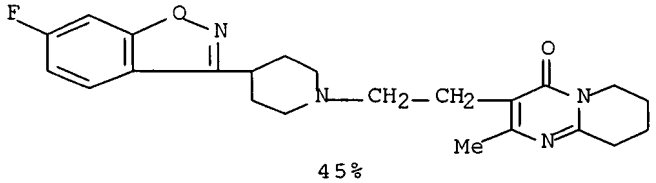
HU 200104873	A2	20030828	HU 2001-4873	20011113
HU 200104873	A3	20031128		
AU 2002363610	A1	20030526	AU 2002-363610	20021113
EP 1461338	A1	20040929	EP 2002-803068	20021113
EP 1461338	B1	20070502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005513019	T	20050512	JP 2003-544048	20021113
AT 361298	T	20070515	AT 2002-803068	20021113
BG 108757	A	20050331	BG 2004-108757	20040611
US 2005004141	A1	20050106	US 2004-495362	20040820
PRIORITY APPLN. INFO.:			HU 2001-4873	20011113
			WO 2002-HU120	20021113

OTHER SOURCE(S): MARPAT 138:401742

AB The invention relates to a process for the preparation of risperidone I, well-known antipsychotic agent, and pharmaceutically acceptable acid addition salts thereof by subjecting the oxime II to ring-closure in the presence of an alkali hydroxide, alkali carbonate or alkali alkoxide in an inert organic solvent, converting the base I thus obtained into an acid addition salt or setting free the base I from an acid addition salt thereof which comprises reacting a halogen derivative III (wherein Hal = halogen) with piperidine oxime derivative IV, or an acid addition salt thereof in the presence of a base, and using by the ring-closure of the oxime II formed a alkanol as inert solvent. The process of the present invention enables the economical preparation of a product having a purity suitable for pharmaceutical purposes.

RX(4) OF 9





45%

CON: overnight, 85 - 90 deg C

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:183834 CASREACT Full-text
TITLE: Preparation of risperidone from 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one and 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole in acetonitrile, isopropanol, methyl ethyl ketone, or isobutanol.
INVENTOR(S): Krochmal, Barnaba; Diller, Dov; Dolitzky, Ben-Zion
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014286	A1	20020221	WO 2001-US25387	20010814
WO 2002014286	A9	20030327		
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CA 2535742	A1	20020221	CA 2001-2535742	20010814
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CA 2549244	A1	20020221	CA 2001-2549244	20010814
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US 2002115673	A1	20020822	US 2001-929808	20010814
US 6750341	B2	20040615		
EP 1317434	A1	20030611	EP 2001-963971	20010814
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JP 3751942	B2	20060308		
NZ 524554	A	20050729	NZ 2001-524554	20010814
EP 1783118	A2	20070509	EP 2007-1138	20010814
EP 1783118	A3	20070523		
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MX 2003PA01337	A	20050630	MX 2003-PA1337	20030213

US 2004229905	A1	20041118	US 2003-669272	20030923
US 7256195	B2	20070814		
JP 2006028192	A	20060202	JP 2005-244095	20050825
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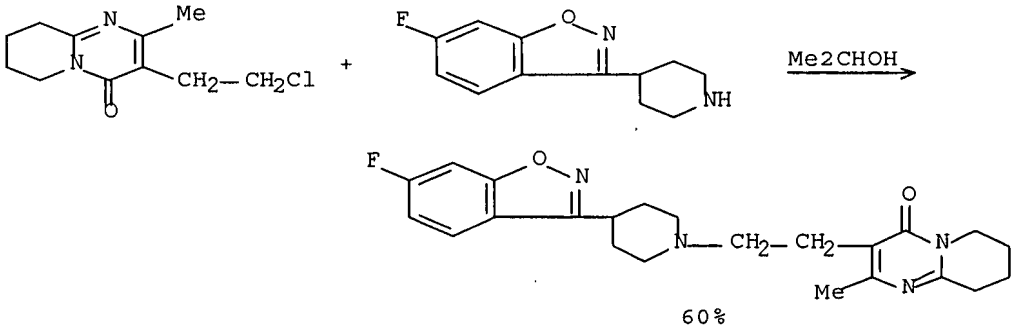
			CA 2001-2535742	20010814
			EP 2001-963971	20010814
			JP 2002-519429	20010814
			US 2001-929808	20010814
			WO 2001-US25387	20010814

AB The title process is claimed. The present invention is directed to preparation of novel crystal forms of risperidone, designated Form A, Form B and Form E. Thus, 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2- a]pyrimidin-4-one, 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole, Na2CO3, and KI were refluxed 9 h in Me2CHOH to give after recrystn. 60% risperidone of 99.7% purity. This was recrystd. from CHCl3/cyclohexane to give risperidone Form B.

RX(1) OF 1



NOTE: reflux, 9 h

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:167385 CASREACT Full-text
TITLE: Preparation of novel polymorphic forms of risperidone
INVENTOR(S): Krochmal, Barnaba; Diller, Dov; Dolitzky, Ben-Zion; Aronhime, Judith
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012200	A1	20020214	WO 2001-US24912	20010808
WO 2002012200	A9	20030403		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 200184763	A	20020218	AU 2001-84763	20010808
US 2002115672	A1	20020822	US 2001-925360	20010808
CA 2535728	A1	20020221	CA 2001-2535728	20010814
CA 2535728	C	20061003		
CA 2535742	A1	20020221	CA 2001-2535742	20010814
CA 2535742	C	20061010		
CA 2549244	A1	20020221	CA 2001-2549244	20010814
CA 2549398	A1	20020221	CA 2001-2549398	20010814
EP 1783118	A2	20070509	EP 2007-1138	20010814
EP 1783118	A3	20070523		

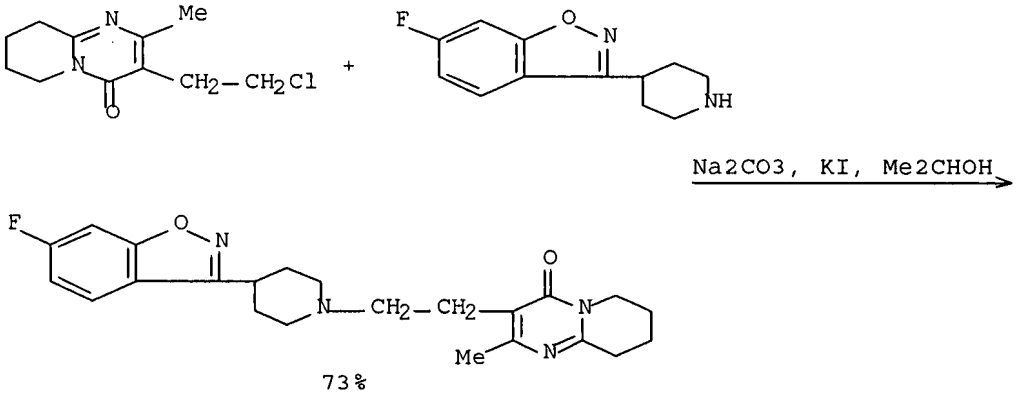
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI

ZA 2003001200	A	20040225	ZA 2003-1200	20030213
US 2004229905	A1	20041118	US 2003-669272	20030923
US 7256195	B2	20070814		
JP 2006028192	A	20060202	JP 2005-244095	20050825
PRIORITY APPLN. INFO.:			US 2000-223779P	20000808
			US 2000-225361P	20000814
			US 2000-243263P	20001025
			WO 2001-US24912	20010808
			CA 2001-2419314	20010814
			CA 2001-2535742	20010814
			EP 2001-963971	20010814
			JP 2002-519429	20010814
			US 2001-929808	20010814

AB The present invention is directed to the novel polymorphic forms of risperidone (I), designated form A, form B and form E, and methods for their preparation The present invention also relates to processes for making risperidone. Pharmaceutical compns. containing the new forms of risperidone and methods of using them are also disclosed. Risperidone (risperdal) is an antipsychotic agent belonging to a new chemical class. It is now found that the synthesis of risperidone from 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole (II) and 3-(2-chloroethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (III) can be carried out in acetonitrile and isopropanol, without using DMF, to give an improved and higher yield of about 75%. The present method eliminates the difficult step of removing DMF from the crude risperidone. The crude risperidone can be efficiently crystallized in high yield from an alc., for example, isopropanol, butanol, ethanol, or methanol, without the need of using the DMF, which is harmful to humans and is a very difficult solvent to remove. Each polymorphic form obtained is characterized by x-ray powder diffraction pattern. Thus, Isopropanol (20 mL), III (2.63 g), II (2.17 g), sodium carbonate (3.18 g), and potassium iodide (66 mg) were added to a 100 mL round bottom flask, and stirred with a magnetic stir bar. The flask was placed in an oil bath at 80° and allowed to reflux for 9 h and then cooled in an ice bath. The content was filtered and the filter cake was washed in the filter with a small amount of isopropanol and then slurried 3 times in 20 mL of water and filtered to give, after drying, 3 g I in 73 % yield. The slurry was recrystd. by dissolving in 37 mL of boiling isopropanol, filtered hot and allowed to cool and filtered to give I with a purity of 99.7 % in an overall yield of 60%. I (5.0 g) was dissolved in methanol (45 mL), followed by adding water (70 mL) to the solution until a

cloudy dispersion was formed. The suspension was filtered to give I filtrate which contained form B polymorph. Further heating of the filtrate overnight at 80° under reduced pressure produced I form A polymorph, which was confirmed by PXRD anal.

RX(1) OF 1



73%

NOTE: alkylation under reflux at 80 degree for 9 h; acetonitrile is also used as the solvent to give 74% crude risperidone; the process avoids the use of DMF as the solvent.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 7 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:357942 CASREACT Full-text
TITLE: A process for the preparation of anti-psychotic 3-{2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl}-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (Risperidone)
INVENTOR(S): Radhakrishnan, Tarur Venkatasubramanian; Sathe, Dhananjay Govind; Suryavanshi, Chandrakant Vasantrao
PATENT ASSIGNEE(S): RPG Life Sciences Limited, India
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085731	A1	20011115	WO 2000-IN53	20000505
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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IN 182944	A1	19990814	IN 1997-BO564	19970926
EP 1280804	A1	20030205	EP 2000-940737	20000505

EP 1280804	B1	20040414			
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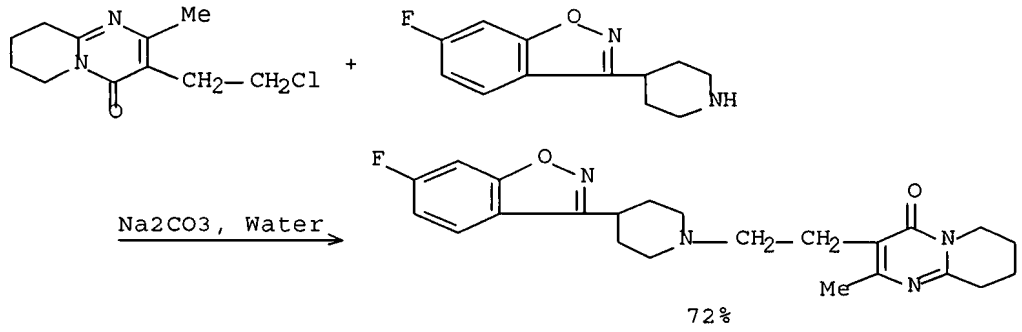
AT 264329	T	20040415	AT 2000-940737	20000505	
US 6897308	B1	20050524	US 2002-257981	20000505	
CZ 295402	B6	20050817	CZ 2002-3666	20000505	
IN 2002MN01520	A	20040911	IN 2002-MN1520	20021030	
PRIORITY APPLN. INFO.:			IN 1997-BO564	19970926	
			WO 2000-IN53	20000505	

OTHER SOURCE(S): MARPAT 135:357942

AB A process for the preparation of 3-(substituted ethyl)-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one I [X = halo, acyloxy, sulfonyloxy such as tosyloxy or mesyloxy], an intermediate in the synthesis of the anti-psychotic risperidone, which comprises hydrogenation of 3-(substituted ethyl)-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one in aqueous inorg. acid medium at atmospheric to 60 psi at 0-100°C in the presence of a metal catalyst. A process for the preparation of risperidone II comprising condensation of I with 6-fluoro-3-(4-piperidinyl)-1,2-benzisoxazole in H2O in the presence of an inorg. base at 25-100°C.

RX(1) OF 3



72%

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 7 OF 7 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	106:67292 CASREACT Full-text
TITLE:	Preparation of 1,2-benzisoxazol-3-yl and 1,2-benzisothiazol-3-yl derivatives as antipsychotics.
INVENTOR(S):	Kennis, Ludo Edmond Josephine; Vandenberk, Jan
PATENT ASSIGNEE(S):	Janssen Pharmaceutica N. V., Belg.
SOURCE:	Eur. Pat. Appl., 33 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

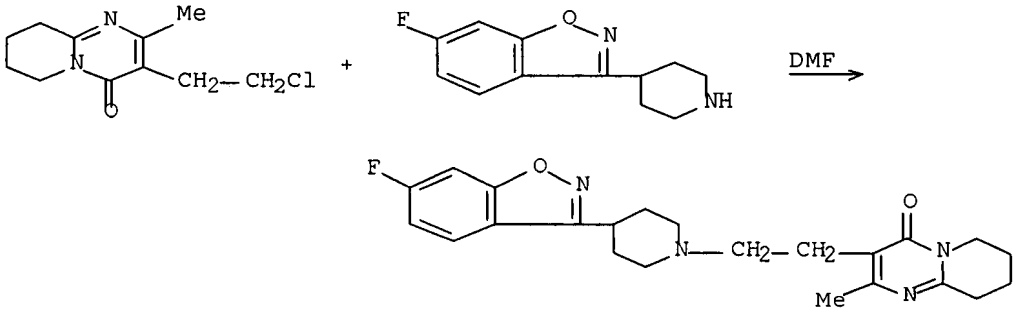
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 196132	A2	19861001	EP 1986-200400	19860313
EP 196132	A3	19880120		
EP 196132	B1	19920812		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4804663	A	19890214	US 1986-826517	19860205
SU 1468419	A3	19890323	SU 1986-4027047	19860305
AT 79379	T	19920815	AT 1986-200400	19860313
CA 1256867	A1	19890704	CA 1986-504409	19860318
CN 86101906	A	19861001	CN 1986-101906	19860324
CN 1022566	B	19931027		
ES 553419	A1	19870516	ES 1986-553419	19860325
IL 78250	A	19910512	IL 1986-78250	19860325
DK 8601439	A	19860928	DK 1986-1439	19860326
DK 168537	B1	19940418		
FI 8601328	A	19860928	FI 1986-1328	19860326
FI 81800	B	19900831		
FI 81800	C	19901210		
NO 8601230	A	19860929	NO 1986-1230	19860326
NO 162765	B	19891106		
NO 162765	C	19900214		
JP 61221186	A	19861001	JP 1986-66108	19860326
JP 06013511	B	19940223		
AU 8655297	A	19861002	AU 1986-55297	19860326
AU 579232	B2	19881117		
HU 42461	A2	19870728	HU 1986-1278	19860326
HU 195793	B	19880728		
ZA 8602279	A	19871125	ZA 1986-2279	19860326
FI 8903001	A	19890619	FI 1989-3001	19890619
CZ 280767	B6	19960417	CZ 1991-3822	19911216
SK 280125	B6	19990806	SK 1991-3822	19911216
PRIORITY APPLN. INFO.:			US 1985-717067	19850327
			US 1986-826517	19860205
			EP 1986-200400	19860313
			FI 1986-1328	19860326

OTHER SOURCE(S): MARPAT 106:67292

AB The title compds. [I; R = H, C1-6 alkyl; R1,R2 = H, halo, OH, C1-6 alkyl, alkoxy; Q = II (R3 = H, halo, C1-6 alkyl, alkoxy, etc.; R4 = H, halo; Y1,Y2 = O, S), III (R5 = H, C1-6 alkyl; A = alkylene, vinylene, etc.; Z = S, CH2, vinylene, etc.); X = O, S; n = 1-4], effective antipsychotic agents, were prepared and incorporated into various pharmaceutical formulations. Heating a mixture of pyrimidine salt IV.HCl 5.3, benzisoxazole V 4.4, Na2CO3 8, and KI 0.1 part in DMF at 85-90° gave 46% I [R = R1 = H, R2 = 6-F, Q = III [R5 = Me, AZ = (CH2)4], X = O, n = 2]. In a selected test with rats, I showed ED50 of 0.02-0.08 μg/kg s.c. against apomorphine-induced phenomena. A formulation containing I 20, Na lauryl sulfate 6, starch 56, lactose 56, colloidal SiO2 0.8, and Mg stearate 1.2 g was made into 1000 hardened gelating capsules.

RX(4) OF 17



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